REMARKS

Claims 1-7 and 11-17 are pending in the instant application. Claims 1-7 have been withdrawn from consideration by the Examiner. Claims 11-17 have been rejected. Claims 1 and 11 have been amended. Claims 3 and 13 have been canceled. Support for these amendments is provided in the specification, for example, at page 7, line 31 and canceled claims 3 and 13. No new matter is added by these amendments. Reconsideration is respectfully requested in light of these amendments and the following remarks.

I. Restriction Requirement

The Examiner maintained the Restriction Requirement mailed February 22, 2008 suggesting that Applicants arguments related to limitations not claimed.

Accordingly, in an earnest effort to advance the prosecution of this case, Applicants have amended claim 1 to recite "the composition comprising an immunologically effective linear peptide fragment of a platelet protein". Support for this amendment is provided in the specification beginning at page 7, line 31.

This amendment clarifies a special technical feature of the instant claims which links Groups I and II and which makes a contribution over teachings of Bowditch.

Accordingly, reconsideration and rejoinder of claims 1-7 is respectfully requested.

II. Objection to Specification

The title and Abstract have been objected to as not specifying the instant claimed subject matter. Thus, in an earnest effort to advance the prosecution of this case and in accordance with the Examiner's suggestion, Applicants have amended the title and abstract to disclose methods of administration.

Withdrawal of this objection is respectfully requested.

III. Rejection of Claims 11, 12 and 17 under 35 U.S.C. 112, first paragraph - Written Description

Claims 11, 12 and 17 have been rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement. The Examiner has acknowledged the specification to discuss at length human platelet antigen. However, the Examiner suggests that the claims encompass allotypic variations of any and all proteins that are

present in platelets, as well as all possible fragments of said platelet proteins.

Accordingly, in an earnest effort to advance the prosecution of this case, Applicants have amended claim 11 to recite administering to a patient an immunologically effective linear peptide fragment of a human platelet antigen (HPA). Support for the amendment is provided in the specification, for example at page 7, line 31, and in claim 13, now canceled.

Withdrawal of this rejection is respectfully requested.

IV. Rejection of Claims 11-17 under 35 U.S.C. 112, first paragraph - Lack of Enablement

Claims 11-17 have been rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

Applicants respectfully traverse this rejection.

At the outset, it is respectfully pointed out that claim 11 has been amended to recite a method for the prevention or management of a condition caused by exposure to an antithetical allele of a platelet by transfusion or during pregnancy by tolerisation, the method comprising administering to a patient an immunologically effective

linear peptide fragment of a human platelet antigen (HPA). Examples of peptides of the present invention are set forth at pages 6-7 of the specification. Formulations for administration and modes of administration are described at page 8. Further, the ability of various exemplary linear peptide fragments of human platelet antigen to stimulate proliferation of human peripheral blood mononuclear cells (PBMCs) isolated from human whole blood is disclosed in detail in the instant specification at, for example, page 8, pages 10-15, and Figures 1 through 8. Stimulation of proliferation of human peripheral blood mononuclear cells ex vivo has been shown to correlate with in vivo efficacy of other tolerogenic treatments such as allergic asthma. See Campbell et al. JEM 2009 downloaded from jem.ruexpress June 17, 2009, a copy of which is provided herewith. In fact, there is a long history of successful tolerance induction in the field of allergy. Specific immunotherapy (SIT) has been in routine clinical practice for allergy treatment for at least 80 years. It is now recognized that this technique is in fact dependent on Th helper tolerance induction, and many groups are exploiting modern understanding of the relevant mechanisms to design more effective or simpler products that exploit the same strategy. See, for example Larché et al.

Nat Med. 2005 Apr;11 (4 Suppl):S69-76, a copy of which is provided herewith.

Accordingly, experiments presented in the instant application constitute a "working example" since stimulation of proliferation of human peripheral blood mononuclear cells ex vivo correlates with the instant claimed method for tolerogenic treatment of a condition caused by exposure to an antithetical allele of a platelet by transfusion or during pregnancy. See MPEP 2164.02.

MPEP 2164.02 is clear; if the art is such that a particular model is recognized as correlating to a specific condition, then it should be accepted as correlating unless the examiner has evidence that the model does not correlate.

It is respectfully submitted that evidence presented by the Examiner regarding correlation of in vitro or in vivo models with treatment in humans is focused on tolerance induction in human diseases that are quite different in terms of underlying etiology from the alloimmune conditions that are the subject of the current invention. In autoimmune diseases such as multiple sclerosis, rheumatoid arthritis, type 1 diabetes, or diseases of disturbed immune homeostasis such as inflammatory bowel disease, there may be defects in tolerance that both predispose to the condition and may, at least in theory, reduce the applicability of

certain approaches to therapeutic tolerance re-induction. These diseases are quite different from those that are the subject of the current invention, where patients have a healthy immune system, but disease arises because of exposure to foreign blood group antigens. In such patients, there will be no defects in the mechanisms of tolerance, which would therefore be amenable to therapeutic manipulation.

Another crucial difference between complex immunological diseases such as type 1 diabetes and inflammatory bowel disease or the complex immunologic response resulting from transplantation and diseases caused by blood group responses is that the target antigens of primary pathological relevance are unequivocally identified only in the latter group. Since tolerance, by definition is antigen specific, it is not surprising that there have been delays in producing tolerance-based treatments for type 1 diabetes, inflammatory bowel disease and organ transplant in humans, until a clearer picture of the relevant antigens emerges. In contrast, where antigens such as HPA-1a are known to be targets for blood group responses, and the inventors have developed approaches to identify the corresponding T helper epitopes, there is no such barrier to

progress. See Barker et al. Immunol Lett. 2007 Jan 15;108(1):20-6, a copy of which is provided herewith.

In *Cross v. Iizuka*, 753 F.2d 1040, 1050, 224 USPQ 739, 747 (Fed. Cir. 1985), the Court held that based upon the relevant evidence as a whole, there is a reasonable correlation between the disclosed *in vitro* utility and an *in vivo* activity, and therefore a rigorous correlation is not necessary where the disclosure of pharmacological activity is reasonable based upon the probative evidence. The relevant evidence as whole herein clearly shows that there is a correlation between the disclosed in vitro utility of stimulation of proliferation of PBMCs by a defined human antigen and prevention or management of a condition caused by exposure to an antithetical allele of a platelet by transfusion or during pregnancy by tolerisation as claimed.

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. See MPEP 2164.01. The instant claimed invention clearly meets this requirement

Withdrawal of this rejection is respectfully requested.

V. Obviousness-type double patenting rejection

Claims 11-17 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16-22 of copending Application No. 12/096,092.

Applicants respectfully traverse this rejection.

MPEP §804(I)(B)(1) states "[i]f a "provisional" nonstatutory obviousness-type double patenting (ODP) rejection is the only rejection remaining in the earlier filed of the two pending applications, while the later-filed application is rejectable on other grounds, the examiner should withdraw that rejection and permit the earlier-filed application to issue as a patent without a terminal disclaimer."

Applicants believe that the amendments and arguments of this response overcome all other pending rejections.

Therefore, since the filing or 371(c) date of the instant application precedes the filing or 371(c) date for U.S. Application Serial No. 12/096,092, Applicants respectfully request in accordance with MPEP §804(I)(B)(1) that the Examiner withdraw this rejection based on the later-filed application.

VI. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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